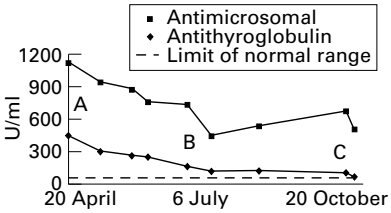
LETTERS TO THE EDITOR

Hashimoto's encephalopathy responding to plasmapheresis

A 47 year old man presented to the emergency department of our hospital. He was born in Uruguay, but had lived in Australia for many years and had not travelled overseas recently. He had no relevant medical history or record of illicit drug use. He had a 2 week history of a coarse, postural tremor of the upper limbs and an unsteady gait and was brought to hospital after an unwitnessed fall at home. On arrival he was alert but "irritable"; shortly thereafter he had a generalised seizure, which was treated with intravenous diazepam and phenytoin. Several hours later he had failed to regain consciousness: he was breathing spontaneously, with roving eyes, absent oculocephalic reflexes, generalised hypertonia and hyperreflexia, bilateral extensor plantar responses, was afebrile, and had no neck stiffness. He was intubated for airway management and had a normal precontrast and postcontrast cerebral CT. A lumbar puncture disclosed normal CSF pressure (15 cm H_2O), with a high protein (1.34 g/l) but normal cell count and glucose. Angiography of the vertebrobasilar system was normal. Intravenous heparin was started, and later intravenous acyclovir. After extubation, he had ongoing cognitive impairment and remained generally hyperreflexic with extensor plantar responses. His admission was characterised by a fluctuating, but slowly improving, delirium. He had short term memory deficits, visual and auditory hallucinations, and paranoid delusions. His upper limb tremor persisted and he had a second generalised seizure. His EEG was diffusely slow without epileptiform activity; this later improved. C-reactive protein was 58 mg/l but other investigations were normal or negative, including routine haematology and biochemistry, erythrocyte sedimentation rate, ANA, ANCA, HIV, and syphilis serology, carotid Doppler studies, brain MRI (precontrast and postcontrast), transoesophageal echocardiography, and CSF culture (including herpes simplex virus polymerase chain reaction). By discharge, his mental function had improved and he was taking clonazepam, phenytoin, carbamazepine, and haloperidol.

He presented again 3 weeks later with worsening generalised tremulousness. He was oriented but distractable. His CSF pressure was raised (21 cm H_2O) and protein was again high (1.06 g/l). Serum B12, folate, and TSH concentrations were normal and anticardiolipin antibodies were negative. His mental state fluctuated dramatically—from coherent, to agitated, to stuporose—often over a 24 hour period; his command of English paralleled his mental state. Despite being euthyroid, his antimicrosomal and antithyroglobulin antibody titres were markedly raised (figure, point A). A diagnosis of Hashimoto's encephalopathy was made and treatment with intravenous methylprednisolone was commenced, followed by oral prednisolone and azathioprine. His level of consciousness improved, as did his memory,



Titres of antithyroid antibodies over a 6 month period. Treatment with corticosteroids and azathioprine was started at diagnosis (A). Plasmapheresis was performed at B and C.

and he was able to perform simple arithmetic. He was discharged from hospital, but 4 weeks later he had not returned to his premorbid level of functioning, with an ongoing tremor and difficulties feeding and dressing himself. Additional treatment was considered necessary, and the patient had a course of plasmapheresis (four exchanges, total 26.8 litres), with the rationale being to remove the presumed pathogenic humoral antibody. The volume of plasma exchanged per treatment was 1.5 times to twice the total plasma volume, and the number of exchanges was consistent with the treatment of other autoimmune neurological disorders.

His condition improved after the first plasma exchange, and by the end of treatment he was able to dress and feed himself and converse in English. He was able to return to part time work as a cleaner. This clinical improvement was accompanied by a further decline in antibody concentrations (figure, point B). He remained well, with slowly rising antibody titres, but when another seizure occurred plasmapheresis (three exchanges, total 21.0 litres) again resulted in a decline in antibody concentrations (figure, point C) and clinical improvement. He continued taking prednisolone and azathioprine throughout this time. He remained euthyroid and had no goitre.

The patient later had a further relapse, associated with generalised seizures. A trial of intravenous gammaglobulin was without effect and his condition again improved promptly with plasmapheresis. When last seen in the outpatient clinic he was clinically well, had no further seizures, and was taking prednisolone, azathioprine, sodium valproate, topiramate, and warfarin. He was building a barbecue at home and his wife thought he was as well as he had ever been. Two days later he was found dead at home by his wife. Initial postmortem examination failed to find a definite cause of death and further pathological investigations are proceeding.

After the initial report by Brain *et al* in 1966,[1] there have been several other individual case reports and series of patients with neurological syndromes associated with high titres of antithyroid antibodies. Our patient followed the typical course described in other cases of Hashimoto's encephalopathy, with tremor and seizures, fluctuating encephalopathy, high CSF protein, and a diffusely abnormal EEG.[2–4] Although abnormalities in brain MRI have been described,[3–5] other patients have had normal MRI,[3 4] as did our patient. The unique feature of the present case was the patient's clinical and serological improvement with plasmapheresis, a treatment that has not been previously described in connection with this condition. The pathogenesis of Hashimoto's encephalopathy remains unclear. Several theories have been proposed, including a generalised abnormality of the immune system, cerebral vasculitis, recurrent demyelination, or a toxic effect of thyrotropin releasing hormone on the CNS.[3 4] It is clear, however, that an abnormality of thyroid function itself cannot explain this condition, as many patients described in the literature are euthyroid either at the time of presentation or relapse. An autoimmune basis is suggested by the high concentrations of antithyroid antibodies and improvement with immunosuppressive therapy. The precise role of antithyroid antibodies is also unclear: if they are to be implicated as pathogenic, then it is surprising that more cases of encephalopathy are not seen in patients with Hashimoto's thyroiditis. It is possible that the antithyroid antibodies in Hashimoto's encephalopathy are a surrogate marker for other, as yet unknown, antibodies that cross the blood-brain barrier and initiate an autoimmune encephalopathy. Various immunosuppressive treatments have been used in this condition, including corticosteroids, azathioprine, cyclophosphamide, and intravenous immunoglobulin.[2 4 5]

This patient's clinical course demonstrates that the response to corticosteroids may be incomplete and that additional clinical and serological improvement can be achieved with the use of plasmapheresis. It is unclear whether the patient's death was related to his underlying neurological condition. If it was, then it is a further indication of the unpredictable course and outcome of Hashimoto's encephalopathy.

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Meningoencephalitis after streptokinase treatment

The mechanisms underlying allergic reactions to streptokinase treatment can be divided into three major groups: immediate IgE mediated (type I), immune complex deposition (type III), and antiorgan antibody mediated (type II). Apart from cerebral haemorrhage the only previously reported neurological complication of streptokinase therapy is the Guillan-Barré syndrome.[1] We present a case of meningoencephalitis after streptokinase therapy.

A 52 year old man presented with classic features of an acute anterior myocardial infarction. Treatment with oral aspirin and intravenous streptokinase was initiated. Fif-